Original article

Classification and management of allergic rhinitis patients in general practice during pollen season

Background: Allergic rhinitis (AR) represents a major challenge in primary care. The Allergic Rhinitis and its Impact on Asthma (ARIA) group proposed a new classification for AR and developed evidence-based guidelines for the management of this disease. We conducted this study to further characterize the classes of AR described by ARIA, and to evaluate whether the management of AR in general practice is in accordance with the ARIA guidelines.

Methods: During the pollen season of 2003, 95 Belgian general practitioners (GPs) enrolled 804 patients who presented with symptoms of AR. For each patient, a questionnaire comprising the clinical presentation and management was completed.

Results: In 64% of the patients, AR was classified as intermittent and in 36% as persistent. Persistent rhinitis caused more discomfort than intermittent rhinitis. Only 50% of the patients had ever undergone allergy testing. Among them, 51% were allergie to both seasonal and perennial allergens. Eighty-two per cent of the persistent rhinitics were allergic to at least one seasonal allergen and 72% of the intermittent rhinitics to at least one perennial allergen. When compared strictly with the ARIA recommendations, 49% of the patients with mild and/or intermittent AR were overtreated, whereas about 30% of those with moderate/severe persistent rhinitis were undertreated.

Conclusion: This study confirms that the previous classification of AR into 'seasonal' and 'perennial' is not satisfactory and that intermittent and persistent AR are not equivalent to seasonal and perennial AR respectively. Furthermore, persistent rhinitis has been shown to be a distinct disease entity. Further efforts are required to disseminate and implement evidence-based diagnostic and treatment guidelines for AR in primary care practice.

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Over the previous decades, the prevalence of allergic disorders has risen to epidemic proportions. Allergic rhinitis (AR) is the most common allergic disease, affecting up to 25% of the population worldwide. As a result of its high and increasing prevalence, its significant impact on quality of life (QoL), its association with multiple comorbidities and the considerable costs in terms of use of healthcare resources, school or work absenteeism and loss of productivity, the disease represents a maior global health concern.

Nevertheless, the burden and consequences of AR are still often underestimated by healthcare providers, patients and their environment. Too often, the disease is underdiagnosed and remains mis- or un(der)treated, which leads to uncontrolled symptoms affecting work, home and social life.

To facilitate and standardize the management of AR and to improve patient care – and consequently, patient satisfaction and compliance – several clinical guidelines have been developed. In 1994 and 2000, European

guidelines for AR (1, 2) were published, recommending a step-wise treatment approach. In 1999, as a result of a WHO initiative, the Allergic Rhinitis and Its Impact on Asthma (ARIA) Working Group was founded. The ARIA guidelines, resulting from this collaboration, are directed towards managing comorbid rhinitis and asthma as manifestations of one 'united airway disease', rather than as two separate diseases of the nose and the lung. They also propose a step-wise treatment strategy for AR, but unlike the European guidelines, the ARIA guidelines are evidence-based (3).

Whereas rhinitis was previously classified into 'seasonal' and 'perennial' (and by extension occupational) based on the type of exposure, the ARIA group reviewed and changed this classification into 'intermittent' or persistent' AR, on the basis of the duration of disease. The gradation of the severity of AR is based on the impact on QoL, rather than on (nasal) symptom scores.

For most patients suffering from AR, the general practitioner (GP) is the (first) point of contact and AR is

identified as one of the top ten reasons for visits to primary care clinics (4). Consequently, the management of AR and the dissemination and implementation of guidelines for AR in general practice receives much attention.

Despite the evidence that a guided strategy is superior to a non-guided one (5), the availability of rigorously developed guidelines does not ensure their use in clinical practice (6). We conducted this survey to evaluate whether the current knowledge regarding diagnostic methods and treatment regimes for AR is applied in daily primary care practice and to further characterize the different classes of AR as described by ARIA.

Materials and methods

Design of the study

In this cross-sectional pharmaco-epidemiological survey, Belgian GPs were asked to recruit consecutive patients who presented at their practice with symptoms of AR during the months February to July 2003, reflecting the tree and grass pollen season. The GPs were instructed to include a maximum of 10 consecutive patients, to allow a fair distribution over the different practices. For every patient, a questionnaire was completed by the GP during the consultation in the questionnaire was designed in order to allow a classification of the patients according to ARIA and included the following items:

- · Patient demographics: age and gender;
- Duration of AR symptoms (number of days per week and number of consecutive weeks per year);
- Impact of AR on the patient's QoL, assessed by the four ARIA questions defining the severity of AR (3);
- Clinical expression of AR and severity of symptoms, measured on a four-point scale, evaluating whether AR is manifested by these symptoms: 1 = never/rarely, 2 = occasionally, 3 = frequently, or 4 = always;
- Most bothersome symptom (rhinorrhoea, nasal congestion, nasal itch, sneezing or conjunctivitis);
- Method of allergy diagnosis [with or without allergy testing: radioallergosorbent test (RAST) and/or skin test];
- · Triggering allergens (confirmed by positive allergy test);
- Treatment prescribed by GP: oral or intranasal antihistamines, nasal decongestants, intranasal or oral glucocorticosteroids, intraocular antihistamines or cromones;
- Referral to specialist.

Patient characteristics, inclusion and exclusion criteria

In order to have an optimal reflection of the AR patient population in daily practice, the exclusion criteria were reduced to a minimum: in daily practice, the exclusion criteria were reduced to a minimum: To avoid data based on hetero-anamnesis, the patients had to be depended as the data of the total of the area of the AR and program women. To avoid data had to be depended as the data of the data

Recruitment of general practitioners

To allow maximal spread, 125 GPs were contacted and asked to participate in a total of 29 different geographical areas covering Belgium. Ninety-five of the 125 GPs contacted agreed to participate, 77.9% males and 22.1% [emales. Among them, 63.8% were in solo practice, and 56.2% in group practice. The distribution of the participating GPs was homogeneous throughout Belgium: 56.8% worked in Flanders, 35.8% in Wallonia and 7.4% in Brussels; 27.4% of the GPs practised in an area with a population density of <2.29 inhabitants/km², 24.2% in an area with 251–500 inhabitants/ M², 25.3% in an area with 501–1000 inhabitants/km² and 23.1% in an area with more than 1000 inhabitants/km² (7). On average, 8.5 patients per investigator were included.

Statistical analyses

The descriptional part of the study uses conventional parameters, mean ± SD for quantitative variables; qualitative variables are represented in terms of percentages. Differences between subgroups are analysed using Chi-square test for nominal or ordinal values, and Kruskal-Wallis test and Mann-Whitney U-test for quantitative values. The significance level was set with an \(\text{ art of } \tex

Results

Duration, severity and ARIA classification of AR

In 36.1% of the patients, symptoms of AR were present for more than four consecutive weeks and during more than 4 days a week. In 42.1%, symptoms of AR were present for four or less consecutive weeks and in 21.8% symptoms of AR were present for more than four consecutive weeks, but only during 5.4 days a week. In accordance with the ARIA classification, 36.1% of the patients were classified with persistent AR and 63.9% were classified with intermittent AR.

Abnormal sleep was reported by 37.1% of the patients, impairment of daily activities, sports or leisure by 71.3%, impairment of work or school by 53.2% and troublesome symptoms by 77.6%. One or more of these four QoL items was (were) disturbed in 89.3% of the patients, who were consequently categorized with moderate/severe thinitis (Table 1)

In the group of persistent rhinities, all four QoL items were more frequently disturbed, when compared with the group of intermittent rhinities. These differences reached significance for abnormal sleep and troublesome symptoms. Consequently, AR was significantly more often graded as moderate/severe in patients with persistent disease than in those with intermittent disease (Table 2).

Table 1. Classification of the patients (n=804) into the four classes, as defined by ARIA

	Persistent	Intermittent	Total
Mild	17 (2.1)	69 (8.6)	86 (10.7)
Moderate-severe	273 (34.0)	445 (55.3)	718 (89.3)
Total	290 (36.1)	514 (63.9)	804 (100)

Values in parentheses represent percentages.

Table 2. Clinical presentation of patients with intermittent vs persistent allergic rhinitis

	Intermittent (n = 514)	Persistent $(n = 290)$	<i>P</i> -value
Male/female	1.05	1.01	NS
Age in years (mean ± SD)	36.1 ± 15.9	36.8 ± 16.5	NS
Impaired sleep (%)	33.5	43.4	0.006
Impaired daily activities/leisure/sports (%)	69.8	73.8	NS
Impaired school/work (%)	51.4	56.6	NS
Troublesome symptoms (%)	73.5	84.8	< 0.001
Moderate/severe AR (%)	86.6	94.1	0.001
Symptom scores (% with score 3 or 4)			
Rhinorrhoea	59.1	59.3	NS
Nasal congestion	58.4	66.2	0.03
Nasal itch	50.2	43.8	NS
Sneeze	61.9	62.4	NS
Conjunctivitis	37.4	43.B	0.09
Headache	11.7	15.5	NS
Somnolence	6.8	13.8	0.002

NS, no statistical significance.

Clinical presentation of AR

Allergic rhinitis was accompanied by sneezing in 89.7% of the patients, by nasal congestion in 86.6%, by rhinorrhoea in 85.9%, by nasal itch in 81.0%, by conjunctivitis in 70.0%, by headache in 48.0% and by somnolence in 37.9% (Fig. 1).

Patients with moderate/severe rhinitis demonstrated significantly higher symptom scores for rhinorrhoea, nasal congestion, nasal itch, conjunctivitis, headache and somnolence compared with those with mild rhinitis

Table 3. Clinical presentation of patients with mild vs moderate/severe allergic rhinitis

	Mild (n = 86)	Moderate/severe (n = 718)	<i>P</i> -value
Male/female	1.05	1.03	NS
Age in years (mean ± SD)	38.8 ± 18.5	36.1 ± 15.8	NS
Symptom scores (% with sco	re 3 or 4)		
Rhinorrhoea	47.7	60.6	0.03
Nasal congestion	39.5	63.8	< 0.001
Nasal itch	32.6	49.7	0.004
Sneeze	58.1	62.5	NS
Conjunctivitis	26.7	41.2	0.01
Headache	5.8	13.9	0.05
Somnolence	0.0	10.4	0.003

NS, no statistical significance,

(Table 3). Patients with persistent rhinitis had significantly higher scores for nasal congestion and somnolence and borderline significantly higher scores for conjunctivitis compared with those with intermittent rhinitis (Table 2).

Of all patients, 38.3% were predominantly bothered by nasal congestion, 28.0% by rhinorrhoea, 17.3% by conjunctivitis, 9.8% by sneezing and 6.6% by nasal itch. Patients predominantly suffering from nasal congestion reported significantly more abnormal sleep than all other patients (42.5% vs 33.7%, P = 0.01), whereas patients especially bothered by conjunctivitis reported more impairment of daily activities, sport and leisure compared with all other patients (78.4% vs 69.6%, P = 0.05) (data not shown).

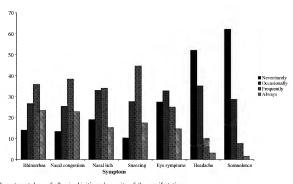


Figure 1. Symptomatology of allergic rhinitis and severity of the manifestations.

Allergy diagnosis and responsible allergens

Of all patients, 47% had never undergone allergy testing to confirm the allergic basis of rhinitis. In 32%, RAST and/or skin tests had been performed in the last 2 years, and in 21% more than 2 years ago. The prevalence of allergy testing was significantly higher in the group of persistent rhinities compared with intermittent rhinities (69.3% vs 44.2%, P < 0.001) and in the moderate/severe group compared with the mild AR group (54.6% vs 41.9%, P = 0.03) (data not shown).

In 351 of the 428 'tested' patients, the cause of allergy was known: 65.2% of the patients were allergic to grass pollen, 63.8% to tree pollen, 63.0% to house dust mite (HDM) and 37.0% to animal dander. No significant differences were found between intermittent and persistent rhinities in the prevalence of allergy caused by grass pollen (65.4% and 65.1%, respectively), tree pollen (62.7% and 53.6%, respectively), HDM (58.4% and 68.1%, respectively) or animal dander (34.6% and 98.%, respectively).

Overall, 50.7% of the patients were allergic to both seasonal (grass and/or tree pollen) and perennial allergens (HDM and/or animal dander). In 82.5% of the persistent rhinities, symptoms were provoked by at least one seasonal allergen (grass and/or tree pollen) and in 71.9% of those classified with intermittent rhinities, AR was triggered by at least one perennial allergen (HDM and/or animals)

Prescribed treatment and specialist referral

None of the patients was on treatment for AR at the time of the visit (was part of the exclusion criteria). At the end of the visit, only one medication was prescribed in 29.6% of the patients, 67.2% received a combination therapy and 3.2% received a no prescription for medication. Overall, topical treatment was recommended in 14.2%, oral therapy in 21.3%, while 61.3% received a combination of oral and topical medication. Oral anti-histamines were the most frequently prescribed pharma-cological agents (82.2%), followed by intranasal glucocorticosteroids (58.2%), nasal decongestants (18.6%), topical eye treatment (intraocular antihistamine or cromone) (17.3%), nasal antihistamines (9.2%) and oral glucocorticosteroids (5.5.%).

Nine per cent of the patients were referred to a specialist. Specialist referral was significantly more often proposed in patients with persistent disease compared with those with intermittent disease, but did not significantly differ between patients with mild or moderate/ severe AR. Remarkably, 27.8% of the patients referred to a specialist did not receive any initial treatment from their GP.

Patients with mild AR more often received no medication than those with moderate/severe AR, but this difference only reached borderline significance. Gluco-

Table 4. Therapeutic management of patients with intermittent vs persistent allergic rhinitis

	Intermittent $(n = 514)$	Persistent $(n = 290)$	P-value
Oral antihistamines (%)	82.1	82.4	NS
Nasal antihistamines (%)	8.8	10	NS
Nasal glucocorticosteroids (%)	53.1	67.2	< 0.001
Oral glucocorticosteroids (%)	4.9	6.2	NS
Nasal decongestants (%)	18.3	19.3	NS
Topical eye medication (%)	14.6	22.1	0.009
No medication prescribed (%)	3.3	3.1	NS
Specialist referral (%)	7.0	12.4	0.01

NS, no statistical significance.

corticosteroids were more often prescribed in persistent rhinities than in intermittent rhinities and in the moderate/severe group compared with the mild group. These differences reached significance for intransas glucocorticosteroids, but not for oral glucocorticosteroids (Tables 4 and 5). We also compared the proposed medication for rhinitis symptoms in the different groups, defined by ARIA, with the recommendations of the ARIA guidelines (Table 6).

Allergic rhinitis treatment in view of the main symptomatology

Among the patients who predominantly suffered from nasal congestion, 70.1% were prescribed an intransal glucocorticosteroid, 20.8% a nasal decongestant and 4.2% an oral glucocorticosteroid, whereas 19.8% received none of these potent anti-congestive agents. Overall, patients who considered nasal congestion as the most bothersome symptom more often received an intransals glucocorticosteroid (70.1% vs 50.6%, P < 0.001) compared with other patients, but no significant differences were found for nasal decongestants or oral glucocorticosteroids (data not shown).

Patients mostly bothered by eye symptoms received an intraocular cromone or intraocular antihistamine in 44.6% of the cases compared with 11.6% in the other patients (P < 0.001); 48.5% did not receive

Table 5. Therapeutic management of patients with mild νs moderate/severe allergic rhinitis

	Mild (n = 86)	Moderate/severe (n = 718)	P-value
Oral antihistamines (%)	62.8	84.5	< 0.001
Nasal antihistamines (%)	8.1	9.3	NS
Nasal glucocorticosteroids (%)	40.7	60.3	< 0.001
Oral glucocorticosteroids (%)	1.2	5.8	NS
Nasal decongestants (%)	22.1	18.2	NS
Topical eye medication (%)	12.8	17.8	NS
No medication prescribed (%)	7.0	2.8	80.0
Specialist referral (%)	7.0	9.2	NS

NS, no statistical significance.

Table 6. Prescribed medication for rhinitis in the different patient groups, classified according to ARIA

	Mild intermittent (n = 69)	Mild persistent (n = 17)		
ND	3 (4.3)	-	5 (1.1)	1 (0.4)
AH	21 (30.4)	4 (23.5)	134 (30.1)	60 (22.0)
AH + ND	15 (21.7)	-	29 (6.5)	10 (3.7)
NGCS	011111111	7 (41.2)	30 (6.7)	16 (5.9)
NGCS + ND	1000	-	4 (0.9)	9 (3.3)
NGCS + AH	10/14/5	6 (35.3)	178 (40)	122 (44.7)
NGCS + AH + ND			22.6.93	25 (9.2)
OGCS				
OGCS + AH	0.00		700	5,000
OGCS + ND			2 (6.4)	
OGCS + AH + ND			4.(6.9)	9,000
OGCS + NGCS			1.66,23	
OGCS + NGCS + AH			671.0	2.67
OGCS + NGCS + ND				1000
OGCS + NGCS + AH + ND			50.0	7.26
No rhinitis medication	7 (10.1)	···	13 (2.9)	12 (4.4)
Treated according to ARIA (%)	56.5	64.7	45.4	63.0
'Undertreated' (%)	10.1 33.3	0.0 35.3	2.9	30.4 8.6

Values in parentheses represent percentages.

ND, nasal decongestant; AH, oral or intranasal antihistamine; NGCS, nasal gluco-corticosteroid; OGCS, oral glucocorticosteroid.

Treated according to ARIA are unshaded; undertreated compared with ARIA recommendations are light shaded; overtreated compared with ARIA recommendations are dark shaded.

topical eye medication, but were prescribed an oral antihistamine for the treatment of their allergic rhinoconjunctivitis.

Discussion

For patients suffering from AR, the GP is often the first point of contact. As many rhinitis patients rely on their GP for the diagnosis and treatment of their symptoms, general healthcare practices represent an interesting and important target to evaluate the management of AR. The ARIA guidelines currently provide diagnostic and thempeutic recommendations for AR with the best evidence. Our study was conducted 2 years after publication of the ARIA document, primarily to assess whether the criteria for diagnosis and the standards for effective treatment are applied in everyday primary care practice (in Belgium).

Whereas ARIA insists on performing highly sensitive and specific in vivo o in viro allergy tests to confirm or exclude an allergic actiology of rhinitis, we found that only half of the patients diagnosed with AR by their GP, had ever undergone allergy testing. In addition, less than 10% were referred to a specialist for further diagnostic or therapeutic management. These figures are similar to

previous results (7, 8), and indicate that GPs do not commonly confirm or support their diagnosis of AR by skin or in vitro allergy tests and rarely ask advice from a specialist. In most cases, the diagnosis of AR is based on a typical clinical picture, consisting of sneezing, nasal congestion, rhinorrhoea, nasal itch and often also conjunctivitis. In our study, these manifestations were part of the symptomatology in 90%, 87%, 86%, 81% and 70% of the patients, respectively. Although allergy tests were not routinely performed, we may assume that the number of falsely diagnosed allergic rhinitics is rather small, as the predictive value of clinical history alone in the diagnosis of AR has been shown to vary between \$2% and \$5% for seasonal allergens and to be at least 77% for perennial allergens.

Similar to other pharmaco-epidemiological trials (7, 10), oral antihistamines were by far the most commonly prescribed first-line medications (82%). Despite previous reports that GPs seem to have some reluctance to use nasal glucocorticosteroids for the treatment of AR (11), we found a rather high prescription rate, especially in patients with persistent (67%) or moderate/severe AR (60%) and in patients predominantly bothered by nasal congestion (70%). Currently, there is no proof for the additional beneficial effects of the combination of an intranasal corticosteroid and an antihistamine compared with an intranasal corticosteroid alone (12), but many experts feel that the former has a superior value (2). This is also reflected in the pharmacological treatment, presented by the GPs in our study, with the combination of these two agents (with or without addition of a nasal decongestant) prescribed in 15% of the mild intermittent, 35% of the mild persistent, 46% of the moderate/severe intermittent and 54% of the moderate/severe persistent rhinitis patients.

Nasal decongestants are very effective for the rapid relief of nasal econgestion, but as they do not improve masal itch, sneezing or rhinorrhoea and hold a significant risk for rebound rhinitis in case of prolonged administration, their use(fulness) is limited. The GPs in our study, nevertheless, prescribed these agents in 20% of the patients and, remarkably, a similar prescription rate was found in patients who were and who were not predominantly bothered by nasal congestion! Oral gluco-corticosteroids, on the other hand, are never recommended as a first-line treatment option for AR, but are preserved for the more treatment-resistant cases of AR. Belgian GPs, however, prescribed them as first-line treatment to 5% of the patients.

In patients with mild and/or intermittent disease, rhinitis symptoms were treated according to the ARIA guidelines in 47% of the cases, were undertreated in only 4%, and were overtreated in 49%. Overtreatment mainly consisted of the prescription of nasal glucocorticosteroids to the mild intermittent group and the combination of a nasal glucocorticosteroid and an antihistamine in the mild persistent and moderate/severe intermittent groups.

It can, however, harely be judged as 'incorrect' to choose the most effective treatment option, when this therapy has proven to be safe and when these agents are available, affordable and acceptable for the patient. For moderate/ severe persistent rhinitis, on the other hand, nasal glucocorticosteroids are the first-choice treatment, but, almost one-third of this patient group was insufficiently treated.

From comparing the treatment strategies proposed by the GPs with the ARIA recommendations, we might conclude that the guidelines are only followed to some extent by the GPs. Of course, it should be recognized that the prescribed treatment is a result of an agreement between doctor and patient, and therefore some deviations from the gold standard are to be expected. In addition, the choice of treatment may also be affected by the presence of comorbid disease or the use of concomitant medication. In patients with comorbid asthma and rhinitis, GPs may prefer to prescribe a systemic treatment that is effective for both manifestations of the united airway disease and leads to increased compliance, instead of a combination of topical treatments. In patients, especially children, already treated with inhaled corticosteroids for asthma, on the other hand, they may want to limit the total glucocorticosteroid dose by choosing other treatment options than intranasal glucocorticosteroids

The results of this survey also allow us to formulate some reflections on the old AR classification, based on the type of exposure, and on the newer ARIA classification, based on the duration of symptoms and their impact on QoL. The inclusion period of our study was limited to the tree and grass pollen season and this trial has an obvious recruitment bias. An overrepresentation of tree pollen- and grass pollen-allergic patients is expected, and this spring survey cannot be used as an epidemiological study to assess the proportion of patients suffering from seasonal or perennial AR. Nevertheless, our results do confirm that the previous classification of AR is not applicable to real-life situations as more than half of the patients had a 'mixed' form of AR, being allergic to both seasonal and perennial allergens. Recently, the ARIA classification has been validated by Demoly et al. in a medical practice-based study in France (13) and by Bauchau et al. in a population-based cross-sectional study in six European countries (14, 15). Both trials demonstrated that perennial allergens can cause intermittent symptoms and that seasonal allergens can cause persistent symptoms. We found 80% of the patients classified with persistent rhinitis to be allergic to tree or grass pollen, and more than 70% of the intermittent rhinitics to be allergic to perennial allergens. These results, together and consistent with the findings of Demoly et al. and Bauchau et al., demonstrate that persistent and intermittent AR are not equivalent to or interchangeable with perennial and seasonal AR, respectively. Furthermore, persistent rhinitis has shown to be clearly different from and more debilitating than intermittent rhinitis. Bauchau et al. reported a greater degree of self-awareness and previous diagnosis, more severe symptoms, a higher rate of doctor-prescribed medication and a more regular use of medication in patients with persistent compared with intermittent rhinitis (15). We found that persistent rhinities had a reduced QoL, marked by an increased rate of troublesome symptoms and impaired sleep, and that they reported more frequent symptoms of somnolence, conjunctivitis and nasal congestion compared with intermittent rhinities. In addition, persistent rhinitis was associated with a higher degree of allergy testing and specialist referral.

Furthermore, in our study, moderate/severe AR was associated with higher symptom scores for nasal congestion, rhinorrhoea, nasal itch, conjunctivitis, headache and somnolence and a higher rate of doctor-prescribed medication compared with mild AR. This demonstrates that the two severity categories for AR defined by ARIA based on the impact of AR on QoL, indeed represent a different burden of disease, also reflected by other outcome measures. Another important observation, however is that, similar to the data of Demoly et al. (7, 10), up to 90% of the patients were categorized with moderate/ severe rhinitis. In addition, Bauchau and Durham reported that 45% of the AR patients in the general population are undiagnosed by a physician and that these previously undiagnosed patients have lower symptom severity (14). It may therefore be suggested that patients consulting their physician are those with moderate/severe rhinitis, whereas those with mild rhinitis often do not seek advice from professional healthcare providers.

Conclusion

This study demonstrates that the ARIA guidelines are often, but not always followed in general practice. To improve the management of a global health problem with increasing prevalence, further efforts are required to disseminate and implement these evidence-based recommendations in primary care practice. In addition, our results support the validity of the ARIA classification and provide more information on the characteristics of AR patients in the different ARIA classification groups. A year-around assessment in the general population, however, is required to make an epidemiologically correct estimation of the proportion of AR patients in the four ARIA classes.

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